GGA	TCC	GGC	TCC	GGA	ACG	GAT	TAC	ACT	CTG	300
Gly	Ser	Gly	Ser	Gly	Thr	дая	Tyr	Thr	Leu	
				70					75	
		AGC								330
Thr	Ile	Ser	Ser		Gln	Pro	Glu	Asp		
				80					85	
		TAT								360
A1a	Thr	Tyr	Tyr		Gln	Asn	Val	Leu		
				90					95	
		TTG		mmo		~~		200		300
		Leu								330
THE	PFO	rea	1111	100	GLY	GIII	GLY	1111	105	
				200					200	
GTG	GAA	ATA	AAA	CGA	ACT	GTG	GCT	GCA	CCA	420
		Ile								
			-	110					115	
TCT	GTC	TTC	ATC	TTC	CCG	. CCA	TCT	GAT	GAG	450
ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	
				120					125	
		AAA								480
Gln	Leu	Lys	Sex		Thr	Ala	Ser	Val		
				130					135	
		CTG								510
Cys	Leu	Leu	Asn		Phe	Tyr	Pro	Arg	G1u 145	
				140					145	
		GTA		moo	***	omo				E 4 0
occ	MAN	OTA	خالاب	100	MIG	016	GWI	MAC	966	540

Ala Lys Val Gln Trp Lys Val Asp Asn Ala 150

95/29697	

165 .

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CTC CAA TCG GGT AAC TCC CAG GAG AGT GTC 570 Leu Gln Ser Gly Asn Ser Gln Glu Ser Val

160

ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC 600 . Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr

170

AGC CTC AGC AGC ACC CTG AGG CTG AGC AAA 630 Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys

180

GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC 660 Ala Asp Tyr Glu Lys His Lys Val Tyr Ala

190

TGC GAA GTC ACC CAT CAG GGC CTG AGC TCG 690

Cys Glu Val Thr His Gln Gly Leu Ser Ser 200

CCC GTC ACA AAG AGC.TTC AAC AGG.GGA GAG 720 . Pro Val Thr Lys Ser Phe Asn Arg Gly Glu 215

TGT TAG

726

Cys

- INFORMATION FOR SEQ ID NO:14: (2)
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 726 base pairs
 - (B) TYPE: Nucleic Acid
 - (C) STRANDEDNESS: Double
 - TOPOLOGY: linear _-(ii) MOLECULE TYPE: Other nucleic acid .
 - DESCRIPTION: 5G1.1 VL +KLV56B
 - (Humanized light chain)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

ATG GGA ATC CAA GGA GGG TCT GTC CTG TTC 30
Met Gly Ile Gln Gly Gly Ser Val Leu Phe
-25 --20

GGG CTG CTG CTC CTC CTG GCT CTC TTC TGC 60 Gly Leu Leu Val Leu Ala Val Phe Cys

-15 - -10

CAT TCA GGT CAT AGC CTG CAG GAT ATC CAG 90 His Ser Gly His Ser Leu Gln Asp Ile Gln -5

1 5

ATG ACC CAG TCC CCG TCC TCC CTG TCC GCC 120 Met Thr Gln Ser Pro Ser Ser Leu Ser Ala

10 19

TCT GTG GGC GAT AGG GTC ACC ATC ACC TGC 150 Ser Val Gly Asp Arg Val Thr Ile Thr Cys 20 25

GGC GCC AGC GAA AAC ATC TAT GGC GCG CTG 180 Gly Ala Ser Glu Asn Ile Tyr Gly Ala Leu 30 . 35

AAC TGG TAT CAA CGT AAA CCT GGG AAA GCT 210 Asn Trp Tyr Gln Arg Lys Pro Gly Lys Ala

CCG AAG CTT CTG ATT TAC GGT GCG ACG AAC 240 Pro Lys Leu Leu Ile Tyr Gly Ala Thr Asn 50 55

CTG GCA GAT GGA GTC CCT TCT CGC TTC TCT 270 Leu Ala Asp Gly Val Pro Ser Arg Phe Ser 60 65

CGA TCC GGC TCC GGA AGG GAT TTC.ACT CTG 300

1. Ser Gly Ser Gly Thr Amp Phe Thr Leuu

70

75

ACC ATC AGC AGT CTG CAG CCT GAA GAC TTC 330

Thr 11e Ser Ser Leu Gln Pro Glu Amp Phe

80

S5

GCT AGG TAT TAC TGT CAG AAC GTT TTA AAT.360

Ala Thr Tyr Tyr Cyr Gln Amn Val Leu Amn

90

55

ACT CCG TTC ACT TTC GGA CAG GGT ACC AAG 330.

Thr Pro Leu Thr Phe Gly Gln Gly Thr Lys

100

105

GTG GAA ATA AAA CGA ACT GTG GCT GCA CCA 420. Val Glu Ile Lys Arg Thr Val Ala Ala Pro 110 ' 115

CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG 480.... Gln Leu Lys Ser Gly Thr Ala Ser Val Val 130

GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC 540 Ala Lys Val Gln Trp Lys Val Asp Asn Ala 150 155 .

CTC CAA TCG GGT AAC TCC CAG GAG AGT GTC 570 Leu Gln Ser Gly Asn Ser Gln Glu Ser Val 160 165 ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC 600

Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr 170 175

AGC CTC AGC AGC ACC CTG ACG CTG AGC AAA 630 Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys

GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC £60 Ala Asp Tyr Glu Lys His Lys Val Tyr Ala 190 195

TGC GAA GTC ACC CAT CAG GGC CTG AGC TCG 690 Cys Glu Val Thr His Gln Gly Leu Ser Ser 200 205

CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG 720 Pro Val Thr Lys Ser Phe Asn Arg Gly Glu 210 215

- (2) INFORMATION FOR SEQ ID NO:15:
 - (A) LENGTH: 711 base pairs
 - (B) TYPE: Nucleic Acid
 - (C) STRANDEDNESS: Double .
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: Other nucleic acid
 - (A) DESCRIPTION:5G1.1 VL + 012

(Humanized light chain)

- 132 - E + 95 - E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15: ATG GAC ATG AGG GTC CCC GCT CAG CTC CTG 30 Met Asp Met Arg Val Pro Ala Gln Leu Leu -20 -15 GGG CTC CTG CTA CTC TGG CTC CGA GGT GCC 60. . . Gly Leu Leu Leu Trp Leu Arg Gly Ala -10-.5 AGA TOT GAT ATC CAG ATG ACC CAG TCC CCG 90 Arg Cys Asp Ile Gln Met Thr Gln Ser Pro 1 TCC TCC CTG TCC GCC ICT GTG GGC GAT AGG 120 Ser Ser Leu Ser Ala Ser Val Gly Asp Arg GTC ACC ATC ACC TGC GGC GCC AGC GAA AAC 150 .. . Val Thr Ile Thr Cys Gly Ala Ser Glu Asn 25 ATC TAT GGC GCG CTG AAC TGG TAT CAA CAG 180 Ile Tyr Gly Ala Leu Asn Trp Tyr Gln Gln AAA CCC GGG AAA GCT CCG AAG .CTT CTG ATT 210 Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile TAC GGT GCG ACG AAC CTG GCA GAT GGA.GTC 240 Tvr Glv Ala Thr Asn Leu Ala Asp Gly Val 50 55 . CCT TCT CGC TTC TCT GGA TCC GGC TCC GGA 270 Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly 60 65

ACG GAT TTC ACT CTG ACC ATC AGC AGT CTG 300 Thr Asp Phe Thr Leu Thr IIe Ser Ser Leu

CAG CCT GAA GAC TTC GCT ACG TAT TAC TGT 330 Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys 80

CAG AAC GTT TTA AAT ACT CCG TTG ACT TTC 360 Gln Asn Val Leu Asn Thr Pro Leu Thr Phe 90 95

GGA CAG GGT ACC AAG GTG GAA ATA AAA CGA 390 Gly Gln Gly Thr Lys Val Glu Ile Lys Arg 100 105

ACT GTG GCT GCA CCA.TCT GTC TTC ATC TTC 420 Thr Val Ala Ala Pro Ser Val Phe Ile Phe 110 115

CCG CCA TCT GAT GAG CAG TTG AAA TCT GGA 450 Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 120 125

ACT GCC TCT GTT GTG TGC CTG CTG AAT AAC 480 Thr Ala Ser Val Val Cys Leu Leu Asn Asn

TTC TAT CCC AGA GAG GCC AAA GTA CAG TGG 510 Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp

AAG GTG GAT AAC GCC CTC CAA TCG GGT AAC 540 Lys Val Asp Asn Ala Leu Gln Ser Gly Asn 150 155 .

	200	

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TCC CAG GAG AGT GTC ACA GAG CAG GAC AGC 570 Ser Gln Glu Ser Val Thr Glu Gln Asp Ser 160

165

AAG GAC AGC ACC TAC AGC CTC AGC AGC ACC 600 Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr

170 175

CTG ACG CTG AGC AAA GCA GAC TAC GAG AAA 630 Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys 185

CAC AAA GTC TAC GCC TGC GAA GTC ACC CAT 660 His Lys Val Tyr Ala Cys Glu Val Thr His 195

CAG GGC CTG AGC TCG.CCC GTC ACA AAG AGC 690 . Gln Gly Leu Ser Ser Pro Val Thr Lys Ser

TTC AAC AGG GGA GAG TGT TAG Phe Asn Arg Gly Glu Cys 210

711

INFORMATION FOR SEQ ID NO:16: (i) SEQUENCE CHARACTERISTICS:

- - (A) LENGTH: 750 base pairs (B) TYPE: Nucleic Acid
 - (C) STRANDEDNESS: Double
 - TOPOLOGY: linear
- (ii) MOLECULE TYPE: Other nucleic acid
 - (A) DESCRIPTION:5G1.1 VH + IGHRLD

(Humanized Fd)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16: .

ATG AAG TGG AGC TGG GTT ATT CTC TTC CTC 30 Met Lys Trp Ser Trp Val Ile Leu Phe Leu .

-15

CTG TCA GTA ACT GCC GGC GTC CAC TCC.CAA 60 Leu Ser Val Thr Ala Gly Val His Ser Gln -5

GTC CAA CTG GTG CAA'TCC GGC GCC GAG GTC 90 Val Gln Leu Val Gln Ser Gly Ala Glu Val

AAG AAG CCA GGG GCC TCA GTC AAA GTG TCC 120 Lvs Lvs Pro Gly Ala Ser Val Lys Val Ser 15

TGT AAA GCT AGC GGC TAT ATT TTT TCT AAT 150 Cys Lys Ala Ser Gly Tyr Ile Phe Ser Asn 25

TAT TGG ATT CAA TGG GTG CGT CAG GCC CCC 180 Tyr Trp Ile Gln Trp Val Arg Gln Ala Pro 35 . . 40

GGG CAG GGC CTG GAA TGG ATG GGT GAG ATC 210 Gly Gln Gly Leu Glu Trp Met Gly Glu Ile

45 TTA CCG GGC TCT GGT AGC ACC GAA TAT GCC 240

Leu Pro Gly Ser Gly Ser Thr Glu Tyr Ala

CAA AAA TTC CAG GGC CGT GTT ACT ATG ACT 270 Gln Lys Phe Gln Gly Arg Val Thr Met Thr 65

					31	890	1 5		PCT/US	N. INECOS	
WO 95/2					21	896	CF		PC170S	15/05688	_
					- 1	36				- '	•
CGT GF	C ACT	TCG ACT	AGT.	ACA	GTA	TAC	ATG	300	-		
Arg As	p Thr	Ser Thr	Ser	Thr	Va1	Tyr 80	Met			-	
		,,				00					
GAG CI	C TCC	AGC CTG	CGA.	TCG	GAG	GAC	ACG	330	-	-	
Glu Le	u Ser	Ser Leu	Arg	Ser	Glu		Thr		. —	2	
		85				90					
GCC GE	C TAT	TAT TGC	GCG	CGT	TAT	TTT	TTT	360 .		-	
Ala Ve	ıl Tyr	Tyr Cys	Ala	Arg	Tyr	Phe	Phe				
		95				100					
GGT TO	T AGC	CCG AAT	TGG	TAT	TTT	CAT	GTT	390			
Gly Se	er Ser	Pro Asn	Trp	Tyr	Phe	Asp	Val				
		105				110					
TGG GG	T CAA	GGA ACC	CTG	GTC	ACT	GTC	TCG	420			
Trp G1	ly Gln	Gly Thr	Leu	Val	Thr	Va,1	Ser				
		115				120					
AGC GC	e rec	ACC AAG	GGC	CCA	TCG	GTC	TTC	450			
Ser Al	la Ser	Thr Lys	Gly	Pro	Ser	Val	Phe				
		125				13.0					
ccc ci	NG GCG	CCC TCC	TCC	AAG	AGC	ACC	TCT	480.			
Pro Le	u Ala	Pro Ser	Ser	Lys	Ser	Thr	Ser				
		135 .				140					
GGG GG	C ACA	GCG GCC	CTG	GGC	TGC	CTG	GTC	510		_	
Gly Gl	ly Thr	Ala Ala	Leu	Gly	Cys	Leu	Val				
		145				150				**	
AAG GA	C TAC	TTC CCC	GAA	CCG	GTG	ACG	GTG	540			
Lys As	p Tyr	Phe Pro	Glu	Pro	Val	Thr	Val		÷		
		155				160					

TCG TGG AAC TCA GGC GCC CTG ACC AGC GGC 570 Ser Tro Asn Ser Glv Ala Leu Thr Ser Glv 165

GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC 600 Val His Thr Phe Pro Ala Val Leu Gln Ser 175

TCA GGA CTC TAC TCC..CTC AGC AGC GTG GTG 630 Ser Gly Leu Tyr Ser Leu Ser Ser Val Val 185

ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG 660 Thr Val Pro Ser Ser Ser Leu Gly Thr Gln 195

ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC 690 Thr Tyr Ile Cys Asn Val Asn His Lys Pro 205 210

AGC AAC ACC AAG GTG GAC AAG AAA GTT GAG 720 Ser Asn. Thr Lys Val Asp Lys Lys Val Glu 215 - 220

CCC AAA TCT TGT GAC AAA ACT CAC ACA TAA 750 Pro Lys Ser Cys Asp Lys Thr His Thr 225

- INFORMATION FOR SEQ ID NO:17:
 - SEQUENCE CHARACTERISTICS: (A) LENGTH: 747 base pairs
 - TYPE: Nucleic Acid (B)
 - STRANDEDNESS: Double
 - (C) TOPOLOGY: linear

 - (ii) MOLECULE TYPE: Other nucleic acid

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(A) DESCRIPTION:5G1.1 scFv.D012 (Humanized scFv)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

1 5 10

TCC TCC CTG TCC SCC TCT GTG GGC GRT AGG 60 Ser Ser Leu Ser Ala Ser Val Gly Asp Arg $15 \hspace{1.5cm} 20 \hspace{1.5cm} ...$

ATC TAT GGC GGG CTG AAC TGG TAT CAA CAG.120

Ile Tyr Gly Ala Leu Asn Trp Tyr Gln Gln

35 40

AAA CCT GGG AAA GCT CCG AAG CTT CTG ATT 150 Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile 45

TAC GGT GCG ACG AAC CTG GCA GAT GGA GTC 180 Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val

CCT TCT CGC TTC TCT. GGA TCC GGC TCC GGA 210 ... Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly

ACG GAT TTC ACT CTG ACC ATC AGC AGT CTG 240 . .

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu 75 80 CAG CCT GAA GAC TTC GCT ACG TAT TAC TGT 270 Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys

85

CAG AAC GTT TTA AAT ACT CCG TTG ACT TTC.300 ...

Gln Asn Val Leu Asn Thr Pro Leu Thr Phe ...

95 100 ...

GGA CAG GGT ACC AAG GTG GAA ATA AAA CGT 330 Gly Gln Gly Thr Lys Val Glu Ile Lys Arg 105 110

ACT GGC GGT GGT GGT TCT. GGT GGC GGT GGA 360 Thr Gly Gly Gly Ser Gly Gly Gly Gly 115

TCT GGT GGT GGC GGT TCT CAA GTC CAA CTG 390 Ser Gly Gly Gly Ser Gln Val Gln Leu 125 130

GTG CAA TCC GGC GCC GAG GTC AAG AAG CCA 420 Val Gln Ser Gly Ala Glu Val Lys Lys Pro 135

GGG GCC TCA GTC AAA GTG TCC TGT AAA GCT 450 Gly Ala Ser Val Lys Val Ser Cys Lys Ala 145 150

AGC GGC TAT ATT TTT TCT AAT TAT TGG ATT 480 Ser Gly Tyr Ile Phe Ser Amn Tyr Trp Ile 155 160

CAA TGG GTG CGT CAG GCC CCC GGG CAG GGC 510 Gln Trp Val Arg Gln Ala Pro Gly Gln Gly 165 170

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CTG GAA TGG ATG GGT GAG ATC TTA CCG.GGC 540 . .

Leu Glu Trp Met Glv Glu Ile Leu Pro Gly 175

TOT GGT AGC ACC GAA TAT GCC CAA AAA TTC 570 Ser Gly Ser Thr Glu Tyr Ala Gln Lys Phe

185

CAG GGC .CGT GTT ACT .ATG ACG CGT GAC ACT 600 Gln Gly Arg Val Thr Met Thr Arg Asp Thr 195

TOG ACT AGT ACA GEA. TAC ATG GAG CTC TCC 630 :...

Ser Thr Ser Thr Val Tyr Met Glu Leu Ser 205 . 210

AGC CTG CGA TCG GAG GAC ACG GCC GTC TAT 660 _ __ Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr

TAT TGC GCG CGT TAT TTT TTT GGT TCT AGC 690 Tyr Cys Ala Arg Tyr Phe Phe Gly Ser Ser 225 230

CCG AAT TGG TAT TTT GAT GTT TGG .GGT. CAA 720. . Pro Asn Trp Tyr Phe Asp Val Trp Gly Gln 235 240

GGA ACC CTG GTC ACT.GTC.TCG AGC TGA 747 Gly Thr Leu Val Thr Val Ser Ser 245

- INFORMATION FOR SEQ ID NO:18:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 5248 base pairs
 - TYPE: Nucleic Acid ... (B)
 - (C) STRANDEDNESS: Double

(ii)

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			- 141 -1
	(D)	TOPOLOGY:	Circular
١		MOLECULE TYPE:	Other nucleic acid

A) DESCRIPTION: pET Trc SO5/NI prokaryotic expression vector

(xi) SEQUENCE DESCRIPTION: SEO ID NO:18:

TOGGRAPHO GACCOCCCC TRACOGGCC ATTAMACCC GCGGGTTGC 50
TOGTTACCCC CAGCOTCAC CTACCCCC ACCCCCCT ACCCCCCCC 10
CCTTICGCTT TCTTCCCTTC.CTTTCTCCC ACCTTCCCC GCTTTCCCC 55
TCAAGCTCTA AATCOGGGC TCCCTTTAGG GTTCCCACTT AGGCCTCACTT ACCCCTTTAC
GCCACCTCGA CCCAAAAAA CTVAATTAGG GTGATGGTTC ACGTAGTGG 30
CCATCGCCCT GATAGACGGT TTTTCGCCCT TTGACGTTCG AGTACACTT 30
CCTTAAATAGT GGACTCTTGT TCCAAACTGG AACACACTC AACCCTATTC 35
CGGTCTATTC TTTTGATTTA TAAGGGATTT TACCGAATTT GGGCTATTG 40
ATTAAAAAAT AGCTGATTTA ACAAAAATTT AACGGAATT TTAACAAAT 55
ACTAAACGTT ACAATTTCAG GTGGCACTT TCGGGGAAAT GTGGGGGGAA 50
CCCCTATTTG TTTATTTTC TAAATACATT CAAATATGAAAAA GTGGGCGGAA 60
AGGAAATAAC CCTGATAAAT GCTCCAATAA TATTGAAAAA GAAGACTAT 60
GAGTATCAA CATTTCCGTG TCGCCCTTAT TCCGTTCTTT CGGGCATTTT 65
GCCTTCCTTT TTTTGCTCC CCAGAAAGC TGGGAGAAGG AAAAGACTCT 70
GAGAACACTAC TTGGGTGCACA AGTGGAAAGG AAAAGACTCT 70
GAGAACACTAC TGGGGCCAC AGTGGGGTTAC ATCGAACACG 75

- 142.

CGGTAAGATC CTTGAGAGTT TTCGCCCCGA AGAACGTTTT.CCAATGATGA ..800 . GCACTITIAA AGTICIGCIA IGIGGGGGGG TATIATCCCG TATIGACGCC...850 GGGCAAGAGC AACTCGGTCG CCGCATACAC TATTCTCAGA ATGACTTGGT . 900 TGAGTACTCA CCAGTCACAG AAAAGCATCT TACGGATGGC ATGACAGTAA .. 950 GAGAATTATG CAGTGCTGCC ATAACCATGA GTGATAACAC TGCGGCCAAC .. 1000 TTACTTCTGA CAACGATCGG.AGGACCGAAG GAGCTAACCG CTTTTTTGCA 1050 CARCATGGGG GATCATGTAA CTCGCCTTGA TCGTTGGGAA CCGGAGCTGA .. 1100 ATGAAGCCAT ACCABACGAC GAGCGTGACA CCACGATGCC TGCAGCAATG .1150 GCAACAACGT TGCGCAAACT ATTAACTGGC GAACTACTTA CTCTAGCTTC . 1200 CCGGCAACAA TTAATAGACT GGATGGAGGC GGATAAAGTT GCAGGACCAC 1250 TTCTGCGCTC GGCCCTTCCG GCTGGCTGGT TTATTGCTGA TAAATCTGGA 1300 GCCGGTGAGC GTGGGTCTCG CGGTATCATT GCAGCACTGG.GGCCAGATGG .1350 TARGCCCTCC COTATCGTAG TTATCTACAC GACGGGGAGT CAGGCAACTA = 1400 TOGATGARCS ARATAGACAS ATCGCTGAGA TAGGTGCCTC ACTGATTAAG .. 1450. CATTGGTAAC TGTCAGACCA AGTTTACTCA TATATACTTT AGATTGATTT . 1500 AAAACTTCAT TTTTAATTTA AAAGGATCTA GGTGAAGATC CTTTTTGATA . 1550. ATCTCATGAC CAAAATCCCT TAACGTGAGT TTTCGTTCCA CTGAGCGTCA 1600 GACCCCGTAG ANAGATCAN AGGATCTTCT TGAGATCCTT TTTTTCTGCG 1650 CGTAATCTGC TGCTTGCAAA CAAAAAAACC ACCGCTACCA..GCGGTGGTTT 1700

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2189015 стттособа теаабаеста селастетт тесебаест алегоесте	1750
AGCAGAGCGC AGATACCAAA TACTGTCCTT CTAGTGTAGC CGTAGTTAGG	1800
CCACCACTTC AAGAACTOTG TAGCACCGCC TACATACCTC GCTCTGCTAA	1850
TCCTGTTACC AGTGGCTGCT GCCAGTGGCG ATAMGTCGTG TCTTACCGGG	1900
TTGGACTCAA GACGATAGTT ACCGGATAAG GCGCAGCGGT CGGGCTGAAC	1950
GGGGGGTTCG TGCACACAGC CCAGCTTGGA GCGAACGACC TACACCGAAC	2000
TGAGATACCT ACAGCGTGAG CTATGAGAAA GCGCCACGCT. TCCCGAAGGG	2050
AGAAAGGCGG ACAGGTATCC GGTAAGCGGC AGGGTCGGAA CAGGAGAGCG	2100
CACGAGGGAG CTTCCAGGGG GAAACGCCTG GTATCTTTAT AGTCCTGTCG	2150
GGTTTCGCCA CCTCTGACTT GAGCGTCGAT TTTTGTGATG CTCGTCAGGG	2200
GGGCGGAGCC TATGGAAAAA CGCCAGCAAC GCGGCCTTTT TACGGTTCCT	2250
GEOCCTTTTGC TEGECETTTTG CTCACATGTT CTTTCCTGCG TTATCCCCTG	2300
ATTCTGTGGA TAACCGTATT ACCGCCTTTG AGTGAGCTGA TACCGCTCGC	2350
CGCAGCCGAA CGACCGAGCG CAGCGAGTCA GTGAGCGAGG AAGCGGAAGA	2400
GCGCCTGATG CGGTATTTTC TCCTTACGCA TCTGTGCGGT ATTTCACACC	2450
GCATATATGG.TGCACTCTCA.GTACAATCTG CTCTGATGCC GCATAGTTAA	2500
GCCAGTATAC ACTCCCCTAT COCTACGTGA CTGGGTCATG GCTGCGCCCC	2550
GACACCCGCC AACACCCGCT GACGCGCCTTG TCTGCTCCCC	2600
COMPONERT ACAGACAGC TOTGACOTO TOGGGAGOT GCATOTGTCA	.2650

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GAGGTTTTCA COGTCATCAC CGARACGCGC GAGGCAGCTG CGGTARAGCT ... 2700 . CATCAGCGTG GTCGTGAAGC.GATTCACAGA TGTCTGCCTG TTCATCCGCG ...2750 . TCCAGCTCGT TGAGTTTCTC CAGAAGCGTT AATGTCTGGC TTCTGATAAA 2800 GCGGGCCATG TTAAGGGCGG TITTTTCCTG TTTGGTCACT GATGCCTCCG. 2850 TGTAAGGGGG ATTTCTGTTC ATGGGGGTAA TGATACCGAT GAAACGAGAG 2900 AGGATGCTCA CGATACGGGT TACTGATGAT GAACATGCCC GGTTACTGGA 2950 ACGTTGTGAG GGTAAACAAC TGGCGGTATG GATGCGGCGG GACCAGAGAA .3000 . AMATCACTCA GGGTCAATGC CAGCGCTTCG TTAATACAGA TGTAGGTGTT .3050 CCACAGGGTA GCCAGCAGCA TCCTGCGATG CAGATCCGGA ACATAATGGT .3100 GCAGGGGGCT GACTTCCGCG TTTCCAGACT TTACGAAACA CGGAAACCGA 3150 AGACCATTCA TOTTGTTGCT CAGGTCGCAG ACGTTTTGCA GCAGCAGTCG $_3200$. CTTCACGTTC GCTCGCGTAT CGGTGATTCA TTCTGCTAAC CAGTAAGGCA . 3250 ACCCCCCCAG CCTAGCCGGG TCCTCAACGA CAGGAGCACG ATCATGCGCA 3300 CCCGTGGGGC CGCCATGCCG GCGATAATGG CCTGCTTCTC GCCGAAACGT 3350 TTGGTGGCGG GACCAGTGAC GAAGGCTTGA GCGAGGGCGT.GCAAGATTCC 3400 GRATACOGCA AGOGACAGGO CGATCATOGT CGCGCTCCAG CGAAAGCGGT .. 3450. CCTCGCCGAA AATGACCCAG AGCGCTGCCG GCACCTGTCC TACGAGTTGC . 3500 ATGATARAGA AGACAGTCAT ARGTGCGGCG ACGATAGTCA TGCCCCGCGC...3550 . CCACCGGAAG GAGCTGACTG GGTTGAAGGC TCTCAAGGGC ATCGGTCGAG. 3600

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ATCCCGGTGC CTAATGAGTG AGCTAACTTA CATTAATTGC GTTGCGCTC	A 3650
CTGCCCGCTT TCCAGTCGGG AAACCTGTCG TGCCAGCTGC ATTAATGAA	T 3700
CGGCCAACGC GCGGGGAGAG GCGGTTTGCG TATTGGGCGC CAGGGTGGT	T 3750
TTTCTTTTCA CCAGTGAGAC GGGCAACAGC TGATTGCCCT TCACCGCCT	ng 3800
GCCCTGAGAG AGTTGCAGCA AGCGGTCCAC GCTGGTTTGC CCCAGCAGC	C 3850
GAAAATCCTG TTTGATGGTG GTTAACGGCG GGATATAACA TGAGCTGTC	T 3900
TOGGTATOGT OGTATOCCAC TACCGAGATA TOCGCACCAA CGCGCAGCC	C 3950
GGACTCGGTA ATGGCGCGCA TTGCGCCCAG CGCCATCTGA TCGTTGGC	AA 4000
CCAGCATCGC AGTGGGAACG ATGCCCTCAT TCAGCATTTG CATGGTTTG	F 4050
TGAAAACCGG ACATGGCACT CCAGTCGCCT TCCCGTTCCG CTATCGGCT	rg 4100
AATTTGATTG CGAGTGAGAT ATTTATGCCA GCCAGCCAGA CGCAGACGC	DG 4150
CCGAGACAGA ACTTANTGGG CCCGCTAACA GCGCGATTTG CTGGTGAC	cc 4200
ARTGCGACCA GATGCTCCAC GCCCAGTCGC GTACCGTCTT CATGGGAG	AA 4250
ANTANTACTG TTGATGGGTG TCTGGTCAGA GACATCAAGA AATAACGC	og 4300
GAACATTAGT GCAGGCAGCT TCCACAGCAA TGGCATCCTG GTCATCCA	GC 4350
GGATAGTTAA TGATCAGCCC ACTGACGCGT TGCGCGAGAA GATTGTGC	AC 4400
CGCCGCTTTA CAGGCTTCGA CGCCGCTTCG TTCTACCATC GACACCAC	CA 4450
CGCTGGCACC CAGTTGATCG GCGCGAGATT TAATCGCCGC GACAATTT	GC 4500
GACGGCGCGT GCAGGGCCAG ACTGGAGGTG GCAACGCCAA TCAGCAAC	GA 4550

CTGTTTGCCC GCCAGTTGTT GTGCCACGCG GTTGGGAATG TAATTCAGCT -4600 CCGCCATCGC CGCTTCCACT TTTTCCCGCG TTTTCGCAGA AACGTGGCTG 4650 GCCTGGTTCA CCACGCGGGA AACGGTCTGA.TAAGAGACAC.CGGCATACTC, 4700 TGCGACATCG TATAACGTTA CTGGTTTCAC ATTCACCACC CTGAATTGAC . 4750. TCTCTTCCGG GCGCTATCAT GCCATACCGC GAAAGGTTTT GCGCCATTCG . 4800 ATGGTGTCCG GGATCTCGAC GCTCTCCCTT ATGCGACTCC.TGCATTAGGA 4850 AGCAGCCCAG TAGTAGGTTG AGGCCGTTGA GCACCGCCGC CGCAAGGAAT ...4900 GGTGCATGCG. GTACCAGCTG TTGACAATTA ATCATCCGGC. TCGTATAATA . 4950 GTACTGTGTG GAATTGTGAG CGCTCACAAT TCCACACATC TAGAAATAAT . 5000 TTTGTTTAAC TTTAAGAAGG AGATATACCA TGGAGATCTG GATCCATCGA 5050. TGAATTCGAG.CTCCGTCGAC AAGCTTGCGG CCGCACTCGA GCACCACCAC 5100 CACCACCACT GAGATCCGGC TGCTAACAAA GCCCGAAAGG AAGCTGAGTT 5150 GGCTGCTGCC ACCGCTGAGC AATAACTAGC ATAACCCCTT GGGGCCTCTA. 5200 AACGGGTCTT GAGGGGTTTT TTGCTGAAAG GAGGAACTAT ATCCGGAT . . 5248

INFORMATION FOR SEQ ID NO:19:

- SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 813 base pairs
 - (B) TYPE: Nucleic Acid
 - (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: Other nucleic acid (A) DESCRIPTION: N19/8 scFv (His Tagged)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

ATG OCC AAT ATT GTG CTG ACC CAA TCT CCA 30

Net Ala Aen Tie Vel Leu Thr Gin Ser Pro

1 5 10

GCT TCT TTG GCT GTG TCT CTA GGG CAG AGG 60

Ala Ser Leu Ale Vel Ser Leu Gly Gin Arg

15 20

GCC ACC ATA TCC TGC AGA GCC AGT GAA AGT 120

Ala Thr Ile Ser Cys Arg Ala Ser Gu Ser

25 30

GTT GAT AGT TAT GAC AAT AGT TTT ATG CAC 150
Val Asp Ser Tyr Asp Asn Ser Phe Met His
35
40

TGG TAC CAG CAG AAA CCA GGA CAG CCA CCC 180
Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro

AAA CTC CTC ATC TTT CTT GCA TCC AAC CTA 210 Lys Leu Leu Ile Phe Leu Ala Ser Asn Leu 55. 60

GAA TCT GGG GTC CCT GCC AGG TTC AGT GGC 240 Glu Ser Gly Val Pro Ala Arg Phe Ser Gly $65 \hspace{1.5cm} 65 \hspace{1.5cm} 70$

AGT GGG TCT AGG ACA GAC TTC ACC CTC ACC 270 Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr 75 80

ATT GAT CCT GTG GAG GCT GAT GAT GCT GCA 300 Ile Asp Pro Val Glu Ala Asp Asp Ala Ala

WO 95/29697

PCT/US95/05688

- 148.-

ACC TAT TAC TGT CAG CAA AAT AAT GAG GTT 330 Thr Tvr Tvr Cvs Gln Gln Asn Asn Glu Val 95 CCG AAC ACG_TTC GGA GGG GGG ACC AAG CTG 360 Pro Asn Thr Phe Gly Gly Gly Thr Lys Leu 105 110 GAA ATA AAA CGG ACC GGA GGT GGC GGG TCG 390 Glu Ile Lys Arg Thr Gly Gly Gly Ser 115... _ 120 GGT GGC GGG GGA TCG GGT GGC GGA GGG TCG 420 Gly Gly Gly Gly Ser Gly Gly Gly Ser 125 130 GAC GTC AAG CTC GTG GAG.TCT GGG GGA GAC 450. Asp Val Lys Leu Val Glu Ser Gly Gly Asp 135 . . 140 TTA GTG ANG CTT GGA GGG TCC CTG ANA CTC 480 Leu Val Lys Leu Gly Gly Ser Leu Lys Leu 145 TCC TGT GCA GCC TCT GGA TTC ACC TTC AGT 510 Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser : . 155 AGC TAT TAT ATG TOT TGG GTT CGC CAG ATT 540 Ser Tyr Tyr Met Ser Trp Val Arg Gln Ile ... 165 170 TCA GAG AAG AGG CTG GAG TTG GTC GCA GCC 570 Ser Glu Lys Arg Leu Glu Leu Val Ala Ala

PCT/US95/05688 2189015

- 149 -

ATT AAT AGT AAT GGT GAT AGC ACC TAC TAT 600 Ile Asn Ser Asn Gly Asp Ser Thr Tyr Tyr 185 190 .

CCA GAC ACT GTG AAG GGC CGA TTC ACC ATC 630 Pro Asp Thr Val Lys Gly Arg Phe Thr Ile . 195 200

TCC AGA GAC AAT GCC AAG AGC ACC CTG GAT 660 ' Ser Arg Asp Asn Ala Lys Ser Thr Leu Asp 205 210

CTG CAA ATG AGC AGT CTG AAG TCT GAG GAC 690 Leu Gln Met Ser Ser Leu Lys Ser Glu Asp 215

ACA GCC TTG TAT TTC TGT GTA AGA GAG ACT 720 Thr Ala Leu Tyr Phe Cys Val Arg Glu Thr 225 230

TAT TAC TAC GGG ATT AGT CCC GTC TTC GAT 750.

Tyr Tyr Tyr Gly Ile Ser Pro Val Phe Asp
235 240

GTC TGG GGC ACA GGG ACC ACG GTC ACC GTC 780
Val Trp Gly Thr Gly Thr Thr Val Thr Val
245
250

TCC TCA CTC GAG CAC CAC CAC CAC CAC CAC 810
Ser Ser Leu Glu His His His His His His His
255 260

TGA

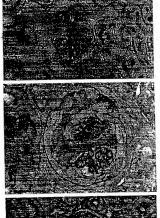


FIG.1A

FIG.1B

FIG.1C

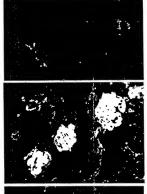


FIG.2A





FIG.2C

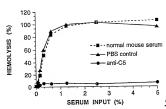
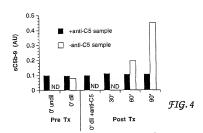


FIG. 3



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FIG.5A

(KOTE STEEL (KOTE SE)

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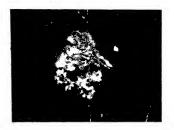


FIG.5B

SUBSTITUTE SHEET (RULE 26)

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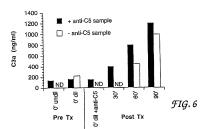
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2189015



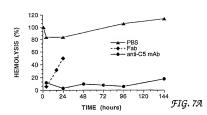
FIG. 5C

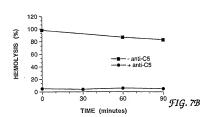
SUBSTITUTE SHEET (RULE 26)



PCT/US95/05688 2189015







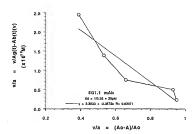


Fig. 8

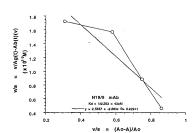


Fig. 9

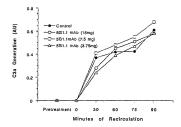


Fig. 10

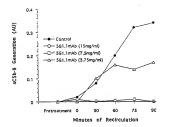


Fig. 11

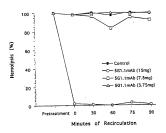


Fig. 12

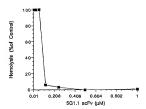


Fig. 13

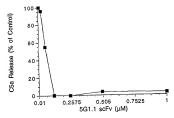


Fig. 14

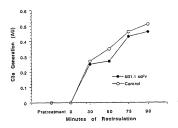


Fig. 15

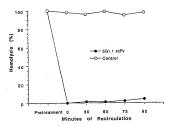


Fig. 16

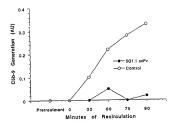


Fig. 17

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Fig. 18

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Fig. 19